this result statistically nonsignificant. The author also had considered nine subdivisions or sub-subdivisions of "leukemia" and found that of 36 deaths, 15 were for "acute myeloid" leukemia versus 8.5 of the 29 expected. These values yielded an SMR of 176 with a 95% confidence interval of 103-285, an apparently statistically significant result. This finding should be considered with respect to the small number of deaths. Thus, despite claims to the contrary by the author, the results of this study do not offer convincing confirmation of those in Milham (1983).

Thomas et al. (1987) analyzed the risk of brain tumor mortality for men occupationally exposed to RFR, lead, and soldering fumes in the petrochemical industry in northern New Jersey, Philadelphia and its surrounding counties, and the gulf coast of Louisiana. Death certificates were obtained for men who had died from brain tumors or other tumors of the central nervous system. One control for each case was selected from men matched in age and year of death and area of residence, but who had died from causes other than brain tumor. Analyses of the estimated maximum-likelihood relative risk (RR) showed significantly elevated RRs for astrocytic brain tumor among men classified as exposed to RFR in jobs involving the design, manufacture, installation, or maintenance of electronic or electrical equipment. RRs were not elevated for exposure to RFR in other types of jobs. On the other hand, the RRs were also higher for electronics workers classified as not having been exposed to RFR. Elevated RRs were also reported for those exposed to soldering fumes, but the variations with presumed exposure level were not large. However, nearly all of those exposed to soldering fumes were engaged in electronics manufacturing and repair jobs. On the basis of the results, the authors suggested that simple exposure to RFR is not the responsible agent for excess brain tumor risk.

Cantor et al. (1995) sought to determine whether a relationship exists between the incidence of female breast cancer and occupational exposure in the U.S. to various substances, ionizing radiation, and radiofrequency and microwave electromagnetic fields. The authors obtained more than 2.5 million mortality records that were coded for occupation from 24 states for the years 1984-1989. For 59,515 white and black female decedents, breast cancer was listed as the underlying cause of death. Four controls per case were randomly selected from all noncancer deaths and were frequency-matched in age, gender, and race. After excluding homemakers, there remained totals of 33,509 case women and 117,794 control women. The authors tabulated 31 potential workplace-exposure agents and created a job-exposure matrix. Two of those 31 categories were for radiofrequency electromagnetic fields and microwave fields. The exposure-probability and the exposure-level results were tabulated separately for the white and black women. The odds ratios (ORs) for almost all of the agents listed were well below 1.2, but for several ORs, the 95% confidence intervals (CIs) exceeded 1.00. As an interesting example, the largest exposure-probability OR in white women was for solder: 2.97 witha 95% CI of 1.3-6.6, but there were only 11 cases and 19 controls. The authors recognized the many limitations of their study, and stated: "...In this investigation, we found no association with either ionizing or nonionizing radiation."

The risk of brain tumor was studied in a relatively large cohort of U.S. Air Force personnel, a fraction of which had exposure to RFR, extremely low frequency fields or ionizing radiation, based on occupational records. The methods for estimating which jobs had potential for relatively large RF exposures to RFR were based on records of incidents of overexposure (above 10 mW/cm^2). This technique led to identification of nearly all jobs involving maintenance and repair of RFR devices, including radar units. After adjusting for an effect of socioeconomic status on brain tumor incidence, the odds ratio for brain tumor was 1.39 (95% CI = 1.01-1.90). This is a weak association which of marginal statistical significance. There was a similar, but not statistically significant association for exposures to extremely low frequency electric and magnetic fields. By contrast, exposures to ionizing radiation showed no

association with brain tumor, but, regardless of any type of exposure, senior officers (representing the highest socioeconomic ranking) had a brain tumor risk of 3.30 (95% CI = 1.99-5.45), a moderate risk with clear statistical significance.

Selvin and colleagues (Selvin et al., 1992) analyzed the clustering of specific childhood cancers in the population of San Francisco for the purpose of determining if there was clustering of childhood cancer near Sutro Tower over the fifteen year period 1973 to 1988. In order to obtain data with the greatest possible statistical power, the authors evaluated population density throughout the city which was divided into census tracts. The average distance to the tower for a child resident in the city ("person at risk") was 3.718 km, a value consistent with the dimensions of the City of San Francisco (approximately 11 km in either the east-west or north-south directions). Selvin et al. (1992) determined that neither childhood leukemia (51 cases), childhood brain cancer (35 cases), nor childhood lymphatic cancer (37 cases) was more common near the tower than elsewhere in the city. This result was found with two types of distance analysis, one using actual distances from the tower and another using distances which were transformed to take population density into account.

Selvin et al. (1992) also did a third analysis which estimated relative risks for a childhood population near the tower in comparison with children living further from the tower. In order to calculate relative risk it was necessary to divide the childhood population into "exposed" and "unexposed" groups. In order to get the best distance for distinction between "exposed" versus "unexposed" cases (that is, the statistically most powerful cutoff distance), the authors devised a model for exposure and tested it for various assumptions about true risk and cutoff distance. They determined that a distance of 3.5 km was best on statistical grounds. In using this distance, the relative risk analysis compared an "exposed" group of approximately 45% of the population under 21 years of age against the remaining 55%. The results agreed with the two distance-based analyses and gave no evidence for increased childhood cancer risk for any of the three cancer categories.

In summary, Selvin et al. (1992) found no evidence by any of three methods that specific childhood cancers were more common near Sutro Tower than elsewhere in the City of San Francisco. As the authors noted, this conclusion needs to be taken with the understanding that potential biases and confounders were not controlled in their analysis. In addition, like all such work, this study could not have detected an excess in childhood cancers below a minimum level. According to a graph presented by the authors, the study had good statistical power (>90% chance of detecting excess risk) if the true risk were about four to five. Therefore, the negative results of this study are evidence that proximity to Sutro Tower is not associated with a risk ratio for each of the three childhood cancers of greater than four to five, but smaller risks might not have been identified.

The incidence of cancer and cancer deaths over the years 1972 to 1990 was analyzed in 3 regions near Sydney, Australia having TV towers in comparison with 6 other nearby regions without TV towers (Hocking et al, 1996). The calculated power densities were from 0.2 to 8 $\mu W/cm^2$ at 4 km from towers and 0.02 $\mu W/cm^2$ at 12 km. In binary comparisons for the zone within 4 km versus the zone from 4 to 12 km, there were statistically significant increases in risks for total leukemia incidence for all ages (odds ratio 1.24, 95% CI = 1.09-1.40) and leukemia incidence in children (odds ratio 1.58 95% CI = 1.07-2.34). Leukemia mortality in children also had a higher odds ratio of 2.32 (95% CI = 1.00-2.41). Brain cancer was not higher for these comparisons. The authors' interpretation of the data is that childhood leukemia was increased among children living close to TV towers. Conclusions from an ecological study design such as this can be in error for many reasons. These include the effects of chance in studies with relatively small

numbers, socioeconomic and environmental cancer risk factors which may be correlated with homes located near TV towers but which have nothing to do with RFR, and incomplete and incorrect assessments of exposure. Exposures can be expected to vary at least as widely as indicated by the calculated values cited in this study. It is difficult to interpret data for which exposure levels for the "exposed group" vary over a forty-fold range. For example, it is probable that some subjects within the 4 to 12 km zone had exposures greater than others within the 4 km zone. Correction for such exposure misclassification could lead to higher or lower odds ratios which, for the number of leukemia cases involved in this study and the relatively small observed increases in risk, might alter the conclusion. However, the finding for childhood leukemia mortality is of moderate strength and if in error, other factors known to influence ecological study designs may be of importance.

The occurrence of a cluster of 12 childhood leukemias in an area of Oahu, Hawaii during the 13 year period from 1979 to 1990 stimulated a study by Maskarinec et al. (1994) to determine if environmental or familial factors might be causally associated with those childhood leukemias. There was particular interest in 7 of the cancers which occurred in just 3 years (1982-1984) and were of unusual types in comparison with most childhood leukemias. The standardized incidence ratio for all leukemia cases was 2.09 (95% CI = 1.08-3.65). The ratios for some specific leukemia types were also greater than one, particularly a ratio of 3.73 (95% CI = 1.20-8.71) for acute nonlymphocytic leukemia (5 cases), a relatively uncommon childhood leukemia. Data obtained since 1985 indicate that there has been no excess of leukemias. The radio towers of interest broadcast at 23.4 kHz, a frequency more than 20,000 times lower than any Sutro Tower DTV transmission. The authors did not indicate if radio emissions differed for the periods before and after 1985. If not, it would be difficult to understand why leukemia rates would drop even if RF exposures were unchanged unless RFR was not a true risk factor for leukemia in this cluster. The influence of possible confounding factors such as exposure to petroleum products, ionizing radiation and socioeconomic status were not given. But some related information was obtained by questionnaire and these factors seemed to be unimportant.

Honolulu, Hawaii was the site of an ecological study of cancer rates for 1979 to 1983 in census tracts near broadcasting towers (Hawaii Department of Health, 1986). The results showed significantly higher rates for all cancers after adjusting for age and race (but not both together). However it was not possible to adjust for smoking, diet or occupational exposures. The SIR for males in the nine census tracts with radio towers was 1.45 and for females 1.27 whereas SIRs for two non-tower tracts were 1.05 (males) and 0.85 (females). The authors noted that leukemia rates (based on a small number of cases) were not significantly higher. The authors adopted a 99 percent confidence interval in the standardized incidence rate for determination of statistical significance ($P < 0.01$). This report, which has not been published in the scientific literature, has no information on RF exposures in the census tracts with radio towers nor a description of the emissions from those towers. As the authors state, an ecological study design such as this where exposures are not well-defined is unlikely to be productive. The results of this study are of little value in assessing any potential hazards of exposure to RFR.

Two recent studies by Dolk et al. (1997a; 1997b) illustrate the difficulties of epidemiologic research concerning cancer clusters (see glossary) and studies using ecological designs. In the first (Dolk et al., 1997a), the authors found greater risk of leukemia among adults living near to the Sutton Coldfield radio transmitter site in England where the mast had both TV and FM radio antennas. For adults living within 2 km of the mast, leukemia risk was significantly higher (odds ratio = 1.83, 95% CI = 1.22-2.74) and risk fell with distance from the transmitter. There were 23 leukemias in the group within 2 km and odds ratios also were greater than 1.0 for most leukemia subtypes, although the small numbers made it difficult to

assess the statistical confidence for each subtype. Total cancers were slightly higher than expected for people older than 15 years of age in homes within both 2 km and 10 km from the mast. Childhood cancer rates were not higher than expected. One indication that these findings were not a statistical oddity is that findings were consistent for two independent time periods: 1974-1980 and 1981-1986. Maximum total power density (summed over frequencies) at 2.5 m above ground were 1.3 $\mu W/cm^2$ for TV and 5.7 $\mu W/cm^2$ for FM. These exposures fell within applicable safety guidelines for public exposure. There were also three industrial sources of pollution within the zone from 3 to 7 km from the mast. The authors concluded that "there was an excess of adult leukemia within the vicinity of the Sutton Coldfield TV/FM transmitter in the period 1974-1986." The authors also concluded, "No causal implications regarding radio and TV transmitters can be drawn from this finding, based as it is on a single 'cluster' investigation."

In order to confirm the validity and generality of this finding the same researchers conducted similar analyses of the incidence of adult leukemia, melanoma, and bladder cancer for 20 additional TV and FM broadcast stations in Great Britain (Dolk et al, 1997b). The results of this study were almost entirely negative: the odds ratio for homes within 2 km of the transmitter was 0.97 (95% CI = 0.78-1.21) and for homes with 10 km the odds ratio was 1.03 (95% CI = 1.00-1.07). When the risk of leukemia was evaluated with respect to distance, there was a borderline finding that risk declined with distance, consistent with the Sutton-Coldfield data. Odds ratios for non-leukemia cancers were not elevated near the transmitters nor was there a decline in odds ratio with distance. The authors concluded that the pattern and magnitude of risk associated with residence near the Sutton Coldfield transmitter did not appear to be replicated around other transmitters. These studies involve exposures which are more like those from the proposed Sutro Tower digital TV transmissions than nearly all other available research, although there are distinctions in the frequencies and modulation patterns. Public health decisions on risk require information from a variety of sources and usually several epidemiology studies. The conflicting results of the two studies by Dolk et al. (1997a; b) illustrate the need for this approach lest true risks be ignored or unconfirmed risks be accepted as if true.

It is seen that most of the epidemiologic studies (including some that reported negative findings) were flawed for various reasons, such as absence of adequate data on RF exposure levels and durations, use of occupational categories as indicative of RF exposure, use of population samples that were too small, utilization of mailed self-administered questionnaires to acquire data, lack of or inappropriate statistical treatment of the data, or incorrect assembly of data bases. It would be misguided to take the results from the foregoing group of studies as evidence on the safety of "RFR" because of the wide disparities in presumed exposure as well as generally poor exposure assessment. A few studies directly address populations near radio and TV towers, but none concerns signals from DTV transmitters operating in the range from approximately 500 to 800 MHz. None of the epidemiologic studies individually provides strong evidence that any particular level or type of RF exposure is carcinogenic, nor does the group of studies lead to this conclusion. However, there is sufficient evidence from occupational research studies to continue investigations of the risk for hematopoietic cancers in highly exposed groups. On the other hand, the evidence for adverse health effects in the general population which is exposed to much lower levels from broadcasting towers is much weaker and, by itself, does not lead to a conclusion that there is an excess risk associated with such exposures. Those data which do suggest effects from low level exposure involve low risk levels and it may be difficult to design studies with good exposure assessment which could make reliable evaluations of risk. Thus, taken collectively, the epidemiologic studies yielded little or no reliable evidence that chronic exposure to RFR at levels within current exposure guidelines is hazardous to human health.

3.2 CONGENITAL ANOMALIES

Two studies were done that sought a possible relationship between the occurrence of Down's syndrome (once called "mongolism") and presumed exposure of the fathers to RFR from radars during military service. In the first study, Sigher et al. (1965) examined the data from Baltimore hospital records and interviews with parents on 216 Caucasian children with Down's syndrome. The case children were matched with 216 control children, as were the parents. One significant finding was that the percentage of case mothers that had received fluoroscopy before the birth of the case child was significantly higher than for the control mothers, as were the percentage of case mothers who had received at least one therapeutic ionizing radiation exposure.

The difference in the percentages of case and control fathers that had served in the military was nonsignificant, but a higher percentage of case fathers had a close association with radars as technicians or operators than the control fathers. The authors therefore ascribed the higher incidence of Down's syndrome primarily to greater exposure of the case mothers to ionizing radiation, but suggested the possibility of a relationship between Down's syndrome and paternal radar exposure.

In the second study, Cohen et al. (1977) reexamined the data in the first study plus the data on 128 additional matched pairs. They concluded that their findings did not confirm the suggestion of a possible association between incidence of Down's syndrome and excess radar exposure of the fathers.

Peacock et al. (1971), in seeking a possible association between the incidence of birth defects in Alabama with the proximity of military bases, examined a state-wide file of birth certificates by counties. They calculated an overall rate of 10.3 newborns with anomalies per thousand births, a rate comparable to those in other registries. However, a more detailed study of the data showed that there were 17 anomalies per thousand births for military personnel in the six-county area surrounding Fort Rocker, whereas the anomaly rate for civilian births was only 6.8 per thousand.

Subsequently, Peacock et al. (1973) reassessed the premise, but with data spanning four years instead of the 17 months examined previously. Also, the data were corrected and rendered more accurate than previously, and a more precise test of the reliability of inferences was performed that did not rely on the questionable use of a normal approximation. The authors then repeated the analyses for the Fort Rocker area and specifically for Lyster Hospital (within Fort Rocker). In addition, as a "control" test, they compared the fetal death anomaly rates in the military hospitals at Fort Rucker and Eglin Air Force Base (which they designated as "radar bases") with those of three military hospitals in bases with minimal radar networks. Those results confirmed that the total anomaly rate and the rates for several specific anomalies were abnormally high at Lyster Hospital. In addition, the numbers of fetal deaths for Lyster and for the hospital at Eglin Air Force Base were comparable and "constitute evidence that the problem may be associated with radar".

Burdeshaw and Schaffer (1977) reexamined the Alabama birth records, but compared the data for Coffee and Dale Counties (within which Fort Rucker is located) with the data from each of the other 65 Alabama counties on a score and rank basis instead of the statewide averages. They found little evidence of unusually high incidence of congenital anomalies in the Fort Rucker area. The increased incidence of congenital anomalies at Lyster Hospital was found to be attributable to a higher than normal reporting rate of one physician who apparently included "birth defects" not regarded as such by other physicians.

Källén et al. (1982) performed a study of 2,043 infants born to Swedish physiotherapists assumed to have been occupationally exposed to various agents such as chemicals, drugs, X-rays, and RFR. The results showed fewer dead or malformed infants than in the general population. The data base was large, so the negative findings are statistically credible.

The authors noted that this excellent outcome could have been because the health of the physiotherapists may have been better than for the general population, a "healthy worker" effect. They hypothesized that more of the relatively few females in the general population who had dead or malformed infants had been subjected to possibly hazardous exposure than those who had normal babies. Accordingly, they also performed a case-control study in which they selected 37 infants who had major malformations or had died perinatally. Each such infant was compared with two normal infants matched for maternal age, parity, and season of delivery. The presumed exposures of the case and control mothers were estimated from answers to a questionnaire. The results indicated that the number of case mothers who had used shortwave equipment was barely higher than for the controls, with statistical probability just within the border of significance ($p=0.05$). However, it should be noted that the difference could have been nonsignificant ($p>0.05$) if one or two answers to the questionnaire were based on faulty recall, so the finding is questionable.

Taskinen et al. (1990) did a study of all registered physiotherapists in Finland who had become pregnant during the study period, to determine whether their occupational exposure to various modalities used for patient treatment, including RFR, is associated with the incidence of spontaneous abortion or of congenital malformations in their offspring. The subjects were those who had been treated for spontaneous abortion or had a malformed child. Data from the responses to questionnaires mailed to 1,329 female physiotherapists on their exposure to various modalities, including ultrasound or shortwaves, and their physical exertions were studied. Based on specific selection criteria, the final populations analyzed were 204 cases of spontaneous abortion with 483 matched controls, and 46 births of congenitally malformed infants with 187 matched births of normal infants.

For assessing the exposures of the therapists, the authors classified the equipments used in treating patients. Exposure duration was defined as the amount of time the therapist handled the equipment during operation while standing at distances of 1 meter or less. The authors used linear logistic regression for individually matched data, and evaluated significance in terms of odds ratios (ORs) relative to estimates based on a normal distribution.

From the data gathered, ultrasound exposure was most often reported (115 cases and 256 controls). Analysis showed that handling ultrasound equipment for at least 20 hours per week increased the risk of spontaneous abortion significantly ($p<0.05$), but those subpopulations were small (9 cases and 8 controls. Administering electric therapies for at least 5 hours per week also showed a significant increase of spontaneous-abortion risk. Physical exertion by the therapists was the only other factor that showed a significant increase of spontaneous-abortion risk. Specifically, heavy lifting (weights exceeding 10 kg) and/or transfer of patients 50 or more times a week yielded a significantly higher OR.

From an analysis by pregnancy duration, heavy lifting during pregnancies 10 weeks or shorter was the only factor that contributed to a significant risk for spontaneous abortion. On the other hand, for pregnancies exceeding 10 weeks, significant risks were indicated for using deep-heat-therapy equipment (including those emitting shortwaves) for 5 or more hours a week. Similar results were obtained for ultrasound and

infrared heating for 10 or more hours a week. The authors regarded these results and the absence of significant risk increases for pregnancy durations 10 weeks or shorter as indicative of a dose-response relationship. Heavy lifting was a significant factor again, but for both ranges of pregnancy duration.

Among the results for congenital malformations (46 cases and 187 age-matched controls) was a significant risk increase for administering shortwave deep-heat therapy for 1-4 hours per week but not for 5 or more hours a week. The authors suggested that bias due to selective recall cannot be excluded in this part of the study, but discounted such bias in the spontaneous-abortion part. No significant risk increase was seen for congenital malformations from the use of microwaves.

In the absence of any data on exposure levels and their variations with time and patient-treatment site, the authors' use of the term "dose" as in "dose-response relationships" is meaningless quantitatively, and their remarks about various other points in their discussion are obscure at best. Thus, at least with regard to RFR, little if any credence can be given to either the positive or negative findings of this study.

Larsen et al. (1991) performed a study of possible reproductive hazards among Danish female physiotherapists from exposure to RFR. The subjects were members of the Union of Danish Physiotherapists who had delivered infants or miscarried. The data for spontaneous abortions, subfecundity, stillbirth or infant death within one year, prematurity, and low birthweight yielded ORs that were nonsignificantly different from 1. The only major positive finding was an unexpected low ratio of boys to girls for the physiotherapists exposed to high-frequency radiation.

The statistical treatments of the data in this study were extensive, but as with other epidemiologic studies, the absence of measurements of the actual RFR levels to which the physiotherapists were exposed and the vague estimates of exposure durations vitiate the credibility of the single positive finding as well as the negative findings. In addition, as remarked by the authors, the results are based on sparse data and must be interpreted with caution.

Ouellet-Hellstrom and Stewart (1993) mailed questionnaires to 42,403 female physical therapists in 1989 whose names were obtained from the American Physical Therapy Association, to assess for possible effects of occupational use of microwave and shortwave diathermy at conception time, and specifically whether an excess risk of miscarriage was associated with exposure to RF and microwave radiation just before conception or during the first trimester of pregnancy. A total of 1,753 case pregnancies and 1,753 matched control pregnancies were studied. Case and control therapists who had not worked during the 6 months prior to and during the first trimester were classified as unexposed. Therapists of each group were classified as exposed if they had been working and had reported using microwave or shortwave diathermy during that time interval. Of the 1,759 pregnancies in each group, there were 209 cases (11.9%) and 167 controls (9.5%) who had any exposure.

The authors remarked that for all pregnancies, the OR increased with the number of exposures and that the trend was significant. However, the 95% CI for the most-exposure durations (more than 20 hours a month) encompassed 1.00, and the 95% CI for the cases and controls with exposures less than 5 hours a month also encompassed 1.00, rendering those ORs nonsignificant. Moreover, the percentages of exposed and control cases were too small yield much statistical power. Nevertheless, the authors concluded that the women were at increased risk of miscarriage from reported use of microwave diathermy six months prior to and during the first trimester of pregnancy, but not from shortwave diathermy. Thus, both the positive and negative findings of this study are dubious.

Collectively there is little or no scientifically reliable evidence that chronic exposure of mothers during pregnancy or of fathers to RFR at levels at or below the ANSI/IEEE (1992) maximum exposure guidelines would cause any anomalies in their offspring.

3.3 RFR AND OCULAR CHANGES IN HUMANS

The cornea and lens of the eye are vulnerable to RFR at high levels because of their surface location and because any heat produced by the RFR is removed less effectively than from other regions of the eye. Indeed, there are several documented early cases of inadvertent exposure to RFR at levels high enough to cause cataracts, and safety measures to avoid such exposure have been defined. It is not possible that members of the public would be exposed to Sutro Tower RFR levels high enough to affect the cornea and lens of the eye.

Cleary et al. (1965) examined Veterans Administration hospital records to determine whether the incidence of cataracts could have been related to occupational RF exposure. They selected 2,946 Army and Air Force veterans of World War II and Korean War, and used military occupational specialties (MOSs) to classify each veteran as a radar worker, a nonradar worker, or one whose specialty could not be discerned. Selected for comparison were 2,164 records of veterans hospitalized for other ailments. In the radar group, they found only 19 persons with cataracts, 2,625 persons without cataracts, and 100 persons with uncertain occupations. In the comparison group, only 21 had cataracts, 1,935 did not, and uncertain occupations for the remaining 83 persons. The small numbers of persons with cataracts in both groups yielded no basis for an association between RF exposure and cataract causation.

Cleary and Pasternack (1966) analyzed the responses to a questionnaire on occupational histories of personnel then currently employed at 16 microwave installations, to differentiate controls from exposure cases. They thereby selected 736 workers as occupationally exposed to RFR, and 559 workers from the same locations and occupational environments (other than RFR) as controls. The authors then derived relative-exposure scores by assigning weights to specific factors related to the types and proximity of the equipment used and usage durations. Using a linear regression model, the authors found that the major increase in eye score with time was due to physiological aging of the lens.

Aurell and Tengroth (1973) investigated 98 persons engaged in industrial development of radar equipment. Of those, 68 had been exposed to microwaves (unspecified frequencies, levels, or durations), comprising persons testing radar equipment and measuring microwave radiations from various klystrons; the remaining 30 persons were from experimental laboratories. The control group consisted of 30 people from the same industry who had never been exposed as far as known.

Two eye specialists examined the groups for visual acuity, their lenses, and their retinas without knowledge of their occupation or exposure. Bar graphs of the numbers of those with opacities larger than 0.5 mm in diameter or with a large concentration of smaller opacities were displayed for those less than 26 years old, and for the 5-year age subgroups 26-30 to 56-60 years. However, there were no control persons older than 41 years. Those younger than 26 years in both groups had no such opacities. Of the 20 persons in the exposed subgroup 26-30 years old, 6 had opacities versus 2 of the 15 controls. The corresponding numbers for those 31-35 years old respectively were 5 of 14 exposed versus none of 4 controls. Similarly, for those 36-40 years old, the corresponding values were 6 of 15 exposed persons versus 1 of 2 controls,

and 2 of 6 exposed persons versus none of 2 controls in the age group 41-45 years. As seen, however, the numbers of exposed and control persons in each age group were small.

Sought in the retinal examinations were lesions of the central region of the fundus that resembled the chorioretinal scars after inflammatory reactions. The results indicated that 19 of the 68 exposed people in the testing group exhibited such lesions, compared with only 1 of the 30 in the control group.

It is difficult to lend credence to the findings of this study, because of the small numbers of persons in each 5-year-age subgroup and the absence of control persons older than 41 years. About the latter, the authors did state: "In the higher age group--over 41 years--it is impossible to separate lens opacities due to microwave exposure from a senile cataract because no controls older than 41 years were examined." However, unclear is why they did not do so, and why only 30 persons were selected as controls versus the 98 exposed. Also, absent were any exposure-level measurements and estimates of exposure durations.

Appleton and coworkers initiated surveys in which they examined the eyes of personnel at Army posts where various types of electronic communication, detection, guidance, and weather equipment were under development, test, and use. In Appleton and McCrossan (1972), they presented results of semiannual examinations conducted between 1968 and 1971 of 226 people employed at Fort Monmouth, New Jersey. After determining the visual acuity of each person, they examined their eyes, and recorded: (1) the number, location, and shape of opacities, if present; (2) similarly for vacuoles; (3) similarly for "posterior subcapsular iridescence" (PSCI), an identifiable polychromatic luster, and (4) absence of all three, results termed "negative".

The experimental group (91 persons) were individuals who had histories of working directly with microwaves as test-development personnel or operators of such equipment. The controls were those employed at the Army post but who denied ever having worked with or been near such equipment (135 persons). The groups were divided into subgroups, with one subgroup each for the 10-year age spans 20-29 through 60-69 years; the size of each subgroup and the number of persons in each of the four examination categories above were tabulated.

In those categories, comparisons of the experimental with the control persons in each age subgroup showed several higher percentages, several lower percentages, and several with no difference. Particularly noteworthy were the larger percentages of negative results (absence of all three categories) for the three younger subgroups (20 to 49 years old) of the experimental group than in the corresponding subgroups of the control group, and the converse for the two older subgroups (50-69 years old). The authors did not present any statistical analysis, so whether the differences were significant or not could not be assessed. However, they concluded that the results did not provide any clinical evidence to support the assumption that cataracts that develop in personnel performing duties near microwave generating equipment are a result of microwave exposure.

In Appleton (1973), the authors added, to the Fort Monmouth data, the results for personnel at White Sands Missile Range, NM, and Fort Bliss, TX, and those subsequently obtained for personnel at Tobyhanna Depot, PA, and Fort Huachuca, AZ, thereby yielding pooled totals of 605 experimental and 493 control personnel. The findings for the larger data base were basically similar to those of the first survey. The final results were tabulated in Appleton et al. (1975a), which encompassed 1,542 experimental and 801 control subjects, who were examined semiannually from 1968 to 1973. The authors concluded that lens damage due to microwave radiation from military equipment has not occurred.

Shacklett et al. (1975) did a similar study of 477 military personnel and civilians with known histories of working near microwave-generating equipment at eight Air Force bases. The authors secured detailed work histories of the individuals, the types of microwave equipment involved, and times spent working around each type. The controls were 340 age-matched persons, with no individual who had a current or past history of work with microwave-generating equipment included. The presence of ocular effects or their absence was recorded, using criteria similar to those of Appleton and coworkers. The tabulated results showed surprisingly high percentages of all three criteria in each age group of both the exposed and control groups, with a trend toward increases with age, but no significant RFR-related differences.

Hollows and Douglas (1984a) examined the lenses of 53 radiolinemen who were occupationally exposed to RFR by erecting and/or maintaining radio, television, and repeater towers throughout Australia. The RFR frequencies ranged from 0.558 to 527 MHz, which includes the Sutro Tower Digital TV transmitters frequencies. The subjects included workers who had maximal cumulative RF exposure but none with cataracts or who had cataracts removed. Measurements of power density close to work areas yielded values in the range 0.08 mW/cm^2 to 4,000 mW/cm^2. The results were statistically compared with those for 39 age-matched controls from the same Australian states who had never been radiolinemen.

The primary ocular finding was "posterior subcapsular cataract (PSC)" in either or both eyes of 11 of the 53 radiolinemen (21%) as compared with 3 of 39 controls (8%); alternatively, PSC was found in both eyes of 19 of the 106 eyes (18%) of the radiolinemen as compared with 6 of the 78 control eyes (8%). The former difference was nonsignificant ($p=0.086$) at the 5% level and the latter was barely significant ($p=0.043$). Also reported, however, was nuclear sclerosis, a type of lens opacity possibly attributable to exposure to solar radiation, in 50 (47%) radiolinemen and 34 (44%) of the controls, so the contribution of RF exposure to the results is unclear.

The various epidemiologic studies on potential ocular effects yielded little or no scientifically reliable evidence that chronic exposure to low levels of RFR (below current exposure guidelines or thresholds determined from animal studies) would cause damage to human eyes.

On rare occasions, accidental exposure to relatively high RFR levels has occurred. For example, Hocking et al. (1988) reported on the exposure of 2 radiolinemen to 4.1-GHz RFR at 4.6 mW/cm^2 and 7 radiolinemen at less than 0.15 mW/cm^2 for up to 90 minutes from an inadvertently activated open waveguide. Ophthalmologic examinations of their eyes showed various eye abnormalities in both groups, but vision was not affected in any of the subjects.

3.4 AUDITORY EFFECTS IN HUMANS

Some humans near some types of pulsed radar transmitters have perceived single pulses or pulse trains of RFR as audible clicks in the head. Frey and coworkers were the first in the U.S. to study this effect, but their theory that it was due to direct brain stimulation by the RFR pulses was disproved by later studies. Instead, much experimental evidence supports the conclusion that an RFR pulse can produce a sharp temperature difference at a boundary between regions of dissimilar dielectric properties in the head, a difference large enough to generate a transient elastic wave that is transmitted by bone conduction to the middle ear, to be perceived as sound. Persons with impaired hearing are unable to hear such clicks, and animals with nonfunctioning inner ears do not exhibit RFR-pulse-induced evoked responses in the brainstem. It is not possible that members of the public would be exposed to Sutro Tower RFR levels high

enough to produce such audible clicks nor do the DTV signals have the characteristics required for the RFR auditory effect.

Cain and Rissman (1978) used 3.0-GHz RFR pulses to investigate the RFR-auditory effect in eight human volunteers. The subjects were given standard audiograms for both air-conducted and bone-conducted sound, and the binaural hearing thresholds were determined for seven of them. Then the subjects were presented with 5-μs, 10-μs, 15-μs, and 20-μs RFR pulses at 1 pulse every 2 seconds. Each subject wore foam ear muffs during exposure, to reduce the ambient noise level (to 45 dB).

In brief summary, only 3 subjects could perceive 15-μs pulses, with a pulse-power-density threshold as low as 300 mW/cm^2; one subject could hear 10-μs pulses, with 225 mW/cm^2 as the threshold; and the thresholds for the other subjects were much higher than 300 mW/cm^2. Thus, 300 mW/cm^2 can be taken as the nominal pulse-power-density threshold for humans to hear pulses having durations of about 10 μs or longer. It is worthy of note that the human volunteers had been exposed to pulses of 3.0-GHz RFR at peak power densities as high as 2,500 mW/cm^2 with no apparent ill effects. It is also important to note that because single pulses of specific characteristics can be perceived, it is not meaningful to calculate time-averaged power densities for two or more widely spaced pulses and to cite such low average values as evidence that the RFR-auditory effect is nonthermal.

3.5 RFR SHOCK AND BURN

People could experience electric shock or tissue burns when coming very near or in contact with metallic objects in the vicinity of transmitters that emit RFR at frequencies below about 100 MHz. The ANSI/IEEE (1992) guidelines include maximum exposure limits for avoidance of such effects. The RF shock effects occur at frequencies lower than Sutro Tower DTV frequencies and would not be relevant to effects from Sutro Tower.

4.0 STUDIES OF RFR EFFECTS IN ANIMALS

4.1 EYE DAMAGE BY RFR IN ANIMALS

Many experiments with animals, such as by Carpenter and coworkers and Guy and coworkers, indicate that ocular damage from RF exposure is a gross thermal effect. Both groups of researchers determined thresholds for ocular damage by plotting the power density versus the shortest exposure duration that caused lens opacities. The resulting curves were rectangular hyperbolas, indicating an inverse relationship between power density and minimum duration. Their curves leveled off horizontally (asymptotically) at an average power density that represents the threshold for ocular damage that may occur for indefinitely long exposure durations. In particular, Guy et al. (1975a) reported a threshold for eye damage in rabbits of roughly 150 mW/cm^2 for exposure durations of 100 minutes or longer. Also especially noteworthy in that study were that exposure to RFR at levels that yield a temperature rise within the eye of about 5°C or more are necessary for thermal eye damage, and that no damage occurs from such RFR levels if the eye is cooled during exposure. Kramar, P, C Harris, AF Emery, and AW Guy (1978) were unable to produce cataracts in monkeys using 2,450 MHz diathermy C applicator even up to 500 mW/cm^2. As noted before, Sutro

Tower DTV RFR levels to which the public could be exposed are below the threshold for thermal damage to the eye.

The results of Stewart-DeHaan et al. (1985) on exposure of lenses to pulsed RFR also are evidence for the thermal basis of eye damage by RFR. Noteworthy is a similar study by Creighton et al. (1987) with continuous wave (CW) as well as pulsed RFR, because the pulsed RFR yielded almost 5 times greater depth of lens damage than the CW RFR under corresponding exposure conditions. The exposure by Foster et al. (1986) of the heads of rabbits to the dominant electric field (TE_{10} mode) in a waveguide system at 2.45-GHz RFR, with the left eye of each rabbit toward the source and its right eye as the control, yielded a threshold power density of 285 mW/cm^2 for ocular damage. The equivalent free-space electric-field intensity (in the TE_{10} mode) was 704 mV/cm.

Kues et al. (1985) reported that exposure of the eyes of anesthetized monkeys to 2.45-GHz CW RFR in weekly 4-hour sessions at 30 mW/cm^2 yielded moderate-to-major changes in the numbers of corneal lesions seen with a specular microscope. The authors determined the local SAR to be 7.8 W/kg. Exposures at 5, 10, or 20 mW/cm^2 did not cause any damage. This study and a later one by Kues and coworkers (1992) appeared to indicate that exposure to pulsed RFR caused more damage than CW RFR at 2.45-GHz. The authors also found that pulsed RFR at 10 mW/cm^2 and 15 mW/cm^2 caused iris damage in the form of increased vascular leakage through the blood-aqueous barrier

In the later study, they investigated the effects of timolol maleate and pilocarpine on the reported RFR-induced iris vascular leakage. Either drug was administered just before RF exposure, and sodium fluorescein was used as the tracer. The results were scored as 1 for no fluorescein leakage, through 4 for significant leakage within the first 3 minutes after tracer injection.

For each drug, a relationship between the RFR/drug-response score and the power density was not readily discernible. For example, with neither drug, the mean score was 1.0 (no effect) for 5 mW/cm^2 and for sham exposure; the mean scores for 10 and 15 mW/cm^2 were 2.1 and 2.8, both significantly higher than for sham exposure but not significantly different from each other. For timolol, the mean scores for 0, 5, 10, and 15 mW/cm^2 were respectively 1.0, 2.7, 2.7, and 3.5; the latter three scores were all significantly higher than for sham exposure, but the scores for 5 and 10 mW/cm^2 were the same, despite the 2:1 power-density difference. Similar results were obtained for pilocarpine Also ambiguous were the mean scores for either drug versus its absence at fixed power densities.

The adequacy of the exposure technique and use of the same monkeys in more than one aspect of the study have been questioned, as has the apparent reversibility of the corneal effect, even though the corneal endothelium of the primate is not known to repair itself through cell division.

Kamimura et al. (1994) endeavored to reproduce the findings of Kues et al. (1985) by exposing monkeys without anesthesia for 4 hours to 2.45-GHz CW RFR at power densities in the range 15.9-43.0 mW/cm^2. The results showed no eye abnormalities, even at levels exceeding the 30-mW/cm^2 threshold reported by Kues et al. (1985).

4.2 AUDITORY EFFECTS IN ANIMALS

Animals as well as humans are able to perceive RFR pulses as apparent sound. The findings of numerous studies with experimental animals indicates that such perception of RFR pulses is due to the induction of thermoelastic waves in the head, rather than by direct brain stimulation by the RFR. As indicated in Section 3.4, because single pulses of specific characteristics can be perceived, it is not meaningful to

calculate time-averaged power densities for two or more widely spaced pulses and to cite such low average values as evidence that the RFR-auditory effect is nonthermal.

4.3 MUTAGENESIS, CYTOGENETIC EFFECTS, AND CARCINOGENESIS

Studies were carried out on various microorganisms, insects, and mammals toward determining whether RFR is mutagenic or carcinogenic. The fruit fly and several species of microorganisms were used in tests for such RFR effects because their short life spans permit the study of many generations, well characterized mutation-prone strains are available in large numbers, and baseline data exist on such strains for various non-RFR mutagenic agents.

In some aspects, carcinogenesis and mutagenesis have been found to be correlated, and many chemicals have been screened for potential cancer-causing properties by testing whether they produce mutations in specific bacteria. For example, agents found to be mutagenic for the bacterium Salmonella are also likely to be carcinogenic. However, not all mutagenic effects are possible indicators of carcinogenic effects and not all carcinogenic effects are necessarily due to mutagenesis. Also studied were possible mutagenic effects of RFR in mammals and mammalian tissues.

4.3.1 Mutagenic And Cytogenetic Effects In Microorganisms and Fruit Flies

In a study by Blackman et al. (1976) with E. coli bacteria, in which mutations can be detected readily, no significant differences in genetic activity were found between cultures exposed to either 1.7-GHz at 2 mW/cm^2 or to 2.45-GHz RFR at 10 or 50 mW/cm^2. Dutta et al. (1979) obtained similar results with cultures of Salmonella exposed to 2.45-GHz RFR at 20 mW/cm^2. Also, Anderstam et al. (1983) exposed strains of both E. coli and Salmonella to 27.12 MHz or 2.45 GHz. Many of the changes were statistically nonsignificant, but the overall trend was toward an RFR-induced increase in growth. Other results were both increases and decreases in mutant counts relative to controls, but most of the differences were not significant.

Pay et al. (1972) exposed male fruit flies for 45 minutes to 2.45-GHz RFR at 6 mW/cm^2 and then mated them with virgin female fruit flies. No significant differences were found between exposed and control groups in mean generation times or brood sizes. Hamnerius et al. (1979) exposed fruit fly embryos of a strain prone to a change in eye pigmentation to 2.45-GHz RFR at about 200 mW/cm^2 for 6 hours. There were no significant differences between exposed and unexposed flies in survival rate or numbers of mutations.

Based on findings such as those above, there is no experimental evidence that exposure to RFR induces mutations in bacteria, yeasts, or fruit flies.

4.3.2 Mutagenic, Cytogenetic and DNA Effects in Mammals and Mammalian Tissues and Cells

The "dominant lethal test" (the occurrence of mutations that result in death of the embryo) has been used to assess whether RFR level is mutagenic. A study by Varma and Traboulay (1976), in which this test was used, showed that exposure of male rodents to 1.7-GHz CW RFR at levels that produce frank heating of the testes (10-50 mW/cm^2) tend to reduce fertility, but that such levels were not mutagenic. Experiments on male fertility in rats by Berman et al. (1980) yielded no evidence of an increase of dominant lethal mutations from 2.45-GHz RFR at power densities up to 28 mW/cm^2. McRee et al. (1981) found no

statistically significant effects of exposure of mice to 2.45-GHz RFR at 20 mW/cm^2 on the induction of sister chromatid exchanges, another sensitive technique for assaying genetic damage from mutagens and carcinogens.

An extensive study by Meltz et al. (1990) on exposure of leukemic mouse cell cultures to pulsed 2.45-GHz RFR, either alone or in combination with the chemical mutagen proflavin, yielded negative findings: The RFR in combination with proflavin produced no statistically significant increase in induced mutant frequency relative to the results for treatment with proflavin alone. In addition, RF exposure alone yielded no evidence of mutagenic action.

Garaj-Vrhovac et al. (1992), assuming that RFR is a mutagen, exposed samples of human blood to 7.7-GHz CW RFR at levels in the range 0.5-30 mW/cm^2 and analyzed lymphocytes therefrom for chromosomal aberrations. They appeared to have obtained positive effects, but the absence of important information regarding their methodology and data treatment limit the reliability of these findings. This is also the case for a study by Fucic et al. (1992) in which the authors reported changes in the size distributions of lymphocyte micronuclei in blood samples from humans occupationally exposed to X-rays, microwaves, or vinyl chloride monomer.

Ray and Behari (1990) reported various effects on rats of exposure to 7.5-GHz pulsed RFR at about 0.6 mW/cm^2 average power density and about 1000 mW/cm^2 peak power density. Also, Sarkar et al. (1994), using the same exposure apparatus as Ray and Behari (1990), exposed mice to 2.45-GHz CW RFR at 1 mW/cm^2 for up to 200 days, and reported changes in DNA samples isolated from the brains and testes. The findings of both studies are questionable for reasons similar to those above.

Among the most provocative recent research has been studies of DNA breakage following 2-hour long exposures of rats to CW and pulsed RFR (2.45 GHz). After exposure was completed, the rat brain was studied by the "comet assay," a relatively recent technique in which, following disruption of the cell's plasma membrane, nuclear DNA is made visible along with any DNA fragments which may have resulted from damage to DNA. DNA fragments occur naturally because of the action of chemically active metabolic by-products (free radicals) and as the result of environmental chemicals and radiation. The comet assay reveals DNA damage at relatively low levels of exposure to ionizing radiation and chemical agents. The comet assay gets its name from the appearance under the microscope of a central cloud of undamaged DNA with a faint tail containing DNA fragments which had been drawn from the nucleus by an electric field. Depending on experimental methods, the comet assay can be used to measure fragments from single-stranded or double-stranded DNA. Damage to double-stranded DNA is considered a better indication of potential damage to chromosomes and other adverse effects which, it can be speculated, could lead to degenerative diseases or cancer. The studies of single- and double-strand breaks (Lai and Singh, 1995; 1996) indicated longer DNA comet tails for brain cells exposed to 2450 MHz microwaves at athermal

SARs (0.6 or 1.2 W/kg). The study of single-stranded DNA indicated generally stronger effects for pulsed RFR in comparison with CW fields and stronger effects at the higher SAR. However, CW RFR had an effect observable shortly after exposure whereas the effects of pulsed RFR were observable only 4 hours later. The 1996 study was conducted only at 1.2 W/kg, but tested for both single- and double-strand breaks. In this study both types of DNA were affected, but there was no difference between the effects of pulsed and CW fields. The temporal pattern of the effects on single-strand DNA was inconsistent with expectations based on acute DNA damage followed by repair. Critics of these experiments have also challenged the extreme alkaline conditions used for preparation of the tissues for analysis of single-strand

breaks and contradictions between the results and expectations drawn from prior research on chemicals and ionizing radiation.

One may speculate that DNA damage of the type observed could led to disruptions of cell functions, cell death and perhaps cancer, but there is no conclusive evidence that any of these potential effects occurs. It remains to be seen if the observed DNA damage can be replicated by others, whether a non-thermal mechanism exists to understand the effects, and how to evaluate any relevance for health effects in exposed animals and human beings. Finally, it would be necessary to evaluate the potential for harm under ordinary conditions of exposure. In particular, Sutro Tower RFR emissions are weaker than the 1 to 2 mW/cm^2 fields used in this study of rats and, at most, are at frequencies one-third as high as used by Lai and Singh.

Cleary et al. (1990) studied the growth of cultured brain tumor cells which had previously been exposed for 2 hours to RF fields at 27 or 2450 MHz. The exposure levels ranged from 5 to 74 W/kg, but the authors considered these in vitro exposure to be nonthermal because the apparatus maintained temperature constant by use of a circulated coolant. Cell growth was estimated by a radioactive technique that measures DNA synthesis. The finding claimed by Cleary et al. was that cell growth rates were affected up to 5 days after exposure, that is in cells several generations removed from the cells exposed originally. There was no direct evidence that the indirect measurement of enhanced DNA synthesis was accompanied by an actual change in cell numbers. The authors also speculated that cell cycle kinetics were affected, again without direct evidence. DNA synthesis was affected most (up to a 2.5-fold increase) by 2.45 GHz RF energy at a SAR = 25 W/kg, with lesser effects for exposures at both higher and lower levels. This study was the focus of much interest because of claims that it demonstrated a nonthermal effect on the growth of brain tumor cells and therefore might be a clue that RF energy in general stimulates cell growth. Stimulation of cell growth rate is a hallmark of many substances that cause cancer and therefore there was the suggestion of a possible link from this result in vitro to cancer in humans, particularly for brain tissue of people exposed to the RF energy of cellular telephone fields. A number of cautionary statements should be considered in order to evaluate this line of speculation: Cleary et al. (1990) did not show a direct effect on cell growth and the observed changes in the radioactive counts may have other explanations; the exposure levels exceeded allowable safety guidelines and may have introduced local temperature increases despite aggressive heat removal; the brain cancer cells used in this research are rarely used in scientific research so that their growth properties are not well known; and most importantly, it is not possible to infer effects on a human being as a result of findings made in studies of cancer cells in the laboratory.

In summary, some of the studies that yielded negative results and others that yielded positive results were questionable because of the likelihood of the presence of uncontrolled non-RFR factors or of other kinds of artifact. In general, there is little if any reliable scientific evidence that exposure of mammals or mammalian tissues to low levels of RFR (e.g., within current exposure guidelines) produces mutagenic or cytogenetic effects therein.

4.3.3 Cancer Induction or Promotion in Animal Experiments

Possible association between chronic RF exposure and the incidence of cancer has been reported in a number of epidemiologic studies (see Section 3.1), but for the reasons stated there, little credence can be given to such findings. On the other hand, other studies specifically directed toward determining whether RFR induces or promotes cancer in animals have been performed.

In an early study by Prausnitz and Susskind (1962) in which 200 mice were exposed to 9.3-GHz pulsed RFR at 100 mW/cm^2, the authors had indicated the occurrence of leukemia (a mistaken description) in both the exposed and control mice, but in more of the exposed mice than the control mice. In a subsequent reanalysis of the primary data, Roberts and Michaelson (1983) concluded that the Prausnitz and Susskind (1962) study provided no evidence that chronic RF exposure does or does not induce cancer.

A study by Skidmore and Baum (1974), in which biological effects were sought from exposure to electromagnetic pulses (EMP) [resembling the RFR from a nuclear blast], yielded negative findings. Almost continuous exposure of 20 female rats to EMP for 38 weeks at a peak electric field of 447 kV/m produced no mammary tumors at age 1 year. Also exposed to the EMP were 50 male mice of a strain known to be susceptible to spontaneous leukemia development between 6 and 12 months of age. After 33 weeks of exposure, 42 of the EMP-exposed mice and 24 of the unexposed control mice survived and were examined for leukemia. Examination of the survivors showed that 9 of the 42 exposed mice (21%) were leukemic whereas 11 of the 24 control mice (46%) were leukemic. However, the sample sizes were too small to ascribe statistical validity to that difference in percentages. Unclear is why about half of the control mice had died, a possible indication that uncontrolled non-RFR factors were present.

Chronic exposures to CW 2450 MHz RFR were reported to enhance the development of mouse skin tumors (Szudzinski et al., 1982). These tumors were initiated by repeated applications of a cancer-causing chemical to the skin of exposed and control mice. In correspondence with the more rapid appearance of tumors, exposed mice survived for markedly shorter periods of time. Whereas the mean survival time for control mice was 331 days, the time for animals exposed to 5 mW/cm^2 (SAR 2 W/kg) was 268 days and among animals exposed to 15 mW/cm^2 (SAR 6 W/kg), mean survival was only 165 days. This protocol and the results indicated that the RF exposures acted as a tumor promoter with a clear dose-response relation. In another arm of the study, the authors found that pre-exposure of mice to 10 mW/cm^2 (SAR 4 W/kg) for 1, 2 or 3 months before the carcinogen applications also enhanced tumor growth and reduced lifespan. As the authors suggested, this protocol and results fit the pattern expected for an agent which inhibits immune system function. Additional studies are needed to demonstrate such an effect on the immune system and a positive finding would conflict with other data on immune function (see section 4.6). The authors stated that the power densities were too low to cause detectable increase of body temperature, but it appears body temperatures were not measured.

Szmigielski et al. (1982) investigated whether exposure to 2.45-GHz RFR at 5 or 15 mW/cm^2: would decrease the resistance to lung cancer cells injected before exposure of Balb/c mice (a naturally resistant strain); increase the incidence of breast tumors in female C_3H/HeA mice (a strain known to have high spontaneous incidence of such tumors); and increase the incidence of skin cancer in male Balb/c mice depilated and painted with a chemical carcinogen (BP). The latter protocol on skin tumors is the same as used by Szudzinski et al. (1982) and some data appear to be repeated in both studies. For comparison, other groups of mice were sham exposed or raised under confinement conditions known to cause a chronic stress syndrome.

In the lung-cancer part of the study, the numbers of neoplastic nodules for those exposed at 5 mW/cm^2 and for those stressed by confinement were comparable, and were between those for the groups exposed at 15 mW/cm^2 and the sham-exposed controls, a positive finding. However, since confinement stress alone was found to increase tumor incidence, it seems likely that the added heat stress from the higher RFR level was responsible for the increases in tumor incidence and not any presumed intrinsic carcinogenic properties of RFR. The results for the breast-cancer part, presented in terms of the mean cancer development times and

mean survival times in 50% of the mice, were analogous, as were those in the skin-cancer part of the study. Again, the RFR-induced increases in skin-cancer incidence at 15 mW/cm^2 relative to 5 mW/cm^2 and confinement stress were probably due to the heat stress at the higher RFR level rather than from any intrinsic properties of the RFR.

Szmigielski et al. (1986) provided a critical review of the world literature on immune cell and immune system responses. They concluded that there was "no convincing evidence" for effects on immune cells tested in vitro under non-thermal conditions. Based upon this observation they argued that the reported in vivo effects are caused by effects on endocrine factors and other means for regulation of the immune system. They also suggest the possibility of a nonspecific stress reaction.

Szmigielski et al. (1986) reported additional studies on tumor development involving the carcinogens di-ethyl-nitroso-amine (DENA) and methyl cholanthrene which led to the conclusion that RFR was not a carcinogen but did function as a tumor promoter. A study showing enhanced cAMP levels in cells was, according to the authors, evidence for nonspecific stress. In summary of animal studies with low level (non thermal) RFR, the authors concluded that tumor promotion was a "general phenomenon."

Santini et al. (1988) sought to determine whether low-level exposure of black mice would affect the development of B16 melanoma from cells injected into the animals or survival times. The authors exposed one group of 15 mice to 2.45-GHz CW RFR at 1 mW/cm^2 for 6 daily sessions per week, 2.5 hours each day, until death (up to 690 hours total). Another group was similarly exposed to 2.45-GHz pulsed RFR at the same average power density. A third group was sham exposed as controls. No statistically significant differences were found among the three groups either in tumor development or survival. Tumor development might have been affected either by a direct influence on the tumor cells, or through effects on the immune system or general health. This study provides evidence that RF exposure did not affect the progression of tumors by any mechanism.

In a comprehensive study by the University of Washington by Chou, CK, AW Guy, LL Kunz, RB Johnson, J Crowley, and JH Krupp (1992) on health and longevity, 100 rats were exposed unrestrained in individual cylindrical waveguides to 2.45 GHz RFR at 0.4 to 0.15 mW/cm^2 over the lifetimes of the exposed animals (except those withdrawn for interim tests and those that expired before the end of the exposure regimen), and 100 rats were concurrently sham exposed. After 13 months, 10 each of the RFR-exposed and sham-exposed rats were euthanized (the interim kill), as were 10 of the 12 RFR-exposed and 10 of the 11 sham-exposed rats that had survived to the end of the 25-month exposure regimen (the terminal kill). The whole body average SAR of 0.4 W/kg was the basis for the ANSI 1982 RF safety guidelines and is the basis for current ANSI/IEEE C95.1-1992 standard for the controlled environment.

Only 3 benign neoplasms occurred in rats younger than 1 year, and those were in the sham group. During the second year, benign neoplasm incidence rose rapidly with age for both the RFR and sham groups, but the differences between the groups at each age of death were nonsignificant.

No primary malignant lesions were found in the rats of either group younger than 1 year, but were found in 2 RFR-exposed and 2 sham-exposed rats at ages 13-18 months, in 9 of the RFR group and 1 of the sham group at ages 19-24 months, and in 7 of the RFR group and 2 of the sham group at ages 25-30 months. Thus, without regard to age, totals of 18 rats with malignancies were found in the RFR group and 5 rats in the sham group, a difference noted by the authors to be statistically significant. However, they indicated that the incidence of each specific primary malignancy in the RFR group was similar to the incidence of

that malignancy reported in the literature for untreated rats of the same strain. Also, the lifespan of the two groups was the same; 12 out of 100 exposed and 11 out of 100 control lived until the last day of the experiment. They stated: "The finding here of excessive malignancies in the exposed animals is provocative; however, when this single finding is considered in light of other parameters evaluated, it is questionable if the statistical difference reflects a true biological activity."

The low energy of RFR precludes damage to DNA such as is produced by x-rays and other forms of radioactivity. As a result, researchers have placed emphasis on the questions concerning the possibility that RFR might enhance tumors by promoting the growth of cells which had already been started along the path to cancer. A part of the long and variable sequence of events which follows initiation of the cancer process is identified as "tumor promotion." Wu and colleagues (Wu et al, 1994) reported on groups of mice exposed to a chemical initiator of colon cancer in combination with a chemical cancer promoter and 2450 MHz RFR at a power density of 10 mW/cm^2 (average SAR 10-12 W/kg). Despite the relatively high levels of exposure there was no evidence that exposures over a five month period for 3 hours daily, 5 days per week, had any influence on colon tumor incidence, size or severity.

Modern genetic techniques permit new types of experimentation through the study of genetically altered, cancer-prone mice. An Australian research team made long-term exposures to a group of 101 female mice from a strain of transgenic mice into whose genome the Pim1 gene had been inserted (Repacholi, et al, (1997). This genetic alteration predisposes the mice to a higher rate of T-cell lymphomas. A useful feature of this model is that the tumors in these mice closely resemble spontaneously arising lymphomas. Exposures to pulse-modulated 900 MHz RFR of the type used for the GSM type of cellular telephone transmission were conducted for two 30 minute periods daily for up to 18 months. Compared to a group of 100 controls, the risk of lymphoma among exposed mice was more than doubled (OR = 2.4) with a high degree of statistical confidence (P = 0.006, 95% CI = 1.3-4.5). Interpretation of this result is made difficult by some of the features of the experiment. First, exposures were made in an unusual apparatus which permitted a wide range of exposures to individual mice and a ten-fold range in average exposures to each group of five exposed mice (0.13 to 1.4 W/kg). Although it appears that the mice received, at most, mildly thermal exposures, a better understanding of the exposures is needed. Second, unlike prior studies with this model system, the mice were allowed to live past the age at which lymphocytic lymphomas occurred with the result that the majority of lymphomas in exposed and control mice were of the non-lymphoblastic type (including a preponderance of B-cell lymphomas) and arose after the mice were 10 months of age. Among the controls there were 22 total lymphomas of which 19 were non-lymphoblastic and 3 lymphoblastic. Among the exposed animals there were 43 total lymphomas of which 37 were non-lymphoblastic and 6 lymphoblastic. If only lymphoblastic tumors were considered, the results of this experiment would be negative. Third, a further complication for the study was the occurrence of severe obesity among both control and exposed mice which could may have influenced absorption of energy and the animal's ability to dissipate RFR heating. Fourth, about 10% of mice developed a severe kidney disease which, in combination with RFR might have influenced the progress of the cancer. Finally, it is not known if results such as these from genetically altered mice have any direct bearing on carcinogenesis, particularly lymphomagenesis in humans who, so far as known, do not carry an activated Pim1 gene. These and other questions should be addressed in studies which attempt to replicate the findings and understand its mechanisms. It should be noted that the pulsed RF fields used in the Australian study differ from Sutro Tower DTV signal waveforms and have power densities (ranging from 0.26 to 1.3 mW/cm^2) which exceed those found anywhere in the environment of Sutro Tower (q.v. calculated power densities, section 3.14 of the EIR).

Collectively, the various RFR-bioeffects investigations lead to the conclusion that exposure of either mammalian or nonmammalian subjects to RFR at levels within current exposure guidelines does not produce mutations or cytogenetic effects. Experiments also show that RFR does not induce or promote specific cancers in animals. However, experimental results in rats exposed to pulsed RFR, mice treated with cancer-causing chemicals, and recent results with genetically altered mice leave open the possibility that under particular experimental conditions RFR at levels which do not cause biologically important degree of tissue heating may influence the course of the cancer process. In the absence of confirmed results, in light of contradictory elements in the research results, and because there are conflicting data showing RFR is not carcinogenic, it is not possible either to firmly dismiss nor accept the hypothesis that RFR can influence cancer. Results with cultured mammalian cells, however, support the conclusion that RFR is not a carcinogenic agent.

Upon consideration of available scientific evidence, and in view of the the signal characteristics for Sutro Tower RFR emissions and the relatively low levels of exposure, the experimental evidence leads to the conclusion that exposure to RFR from the Sutro Tower Digital TV transmitters would not cause mutations, cytogenetic effects nor cancer in the general population.

4.3.4 *In Vitro* Cancer Initiation or Promotion

Balcer-Kubiczek and Harrison (1991) exposed cultures of mouse-embryo-fibroblast cells for 24 hours to 2.45-GHz RFR alone at an SAR of 0.1, 1, or 4.4 W/kg, or to the RFR at 4.4 W/kg before or after exposure to X-rays at 0.5, 1, or 1.5 Gy. After such treatments, they incubated the cultures with or without a known tumor promotor (TPA) and then assayed them for the incidence of neoplastic transformations by counting the number of transformed foci in culture dishes.

RF exposure alone produced no evidence of tumor promotion, but the mean neoplastic transformation incidence was higher for the RFR-exposed cultures incubated with TPA. The results were regarded by the authors as indicating that RFR acts to initiate neoplastic transformation. However, the numbers of foci found relative to the numbers of dishes treated were small, the counting was apparently not done without prior knowledge of the treatment of each dish, and the numbers of dishes used for each treatment differed considerably. The latter point raises the question whether the authors may have increased the number of dishes for each treatment until they obtained adequate percentages of foci for statistical analysis. Also open to question is how well were the culture temperatures controlled, particularly at 4.4 W/kg.

4.4 TERATOGENESIS

Teratogenesis refers to the causation of anatomical aberrations (terata) in a developing fetus, but more generally also includes fetal death and/or resorption and postnatal abnormalities in the offspring. Such effects occur naturally at low rates in most mammals, and relatively little is known about their causes. In a few cases, however, specific agents have been shown to cause significant effects, and hence the possibility that such effects could occur from exposure to RFR is an appropriate matter of public concern. The term is usually applied to mammalian fetuses and infants, but effects on nonmammalian subjects also have been sought.

4.4.1 Insects

Various studies were done with pupae of the darkling beetle. In studies by Carpenter and Livstone (1971) at 10 GHz and by Lindauer et al. (1974) and Liu et al. (1975) at 9 GHz, in which pupae were exposed at relatively high power densities, the percentages of abnormal beetles were much higher than from sham-exposed pupae. Carpenter and Livstone (1971) also reported that the percentages of abnormal beetles were much higher from RFR-exposed pupae than from pupae conventionally radiantly heated to the same temperature, which led the authors to conclude that abnormal development of RFR-exposed pupae could not be explained as a thermal effect. However, Pickard and Olsen (1979) found that the percentages of abnormal control beetles obtained from two different suppliers differed significantly, in part because the food given by each supplier to the larvae from which their pupae were derived differed from one another, an indication that uncontrolled non-RFR factors may have been present in the experiments. In addition, Olsen and Hammer (1982), in using scanning thermography on RFR-exposed pupae, found large variations of local SAR within them that would not occur with the radiant heating used by Carpenter and Livstone (1971). Thus, the non-thermal hypothesis of Carpenter and Livstone (1971) remained unproved.

4.4.2 Birds

McRee and coworkers performed a variety of studies on Japanese quail, in which the effects of exposure to 2.45-GHz RFR of arrays of eggs were examined. Among the effects sought were: hatchability, percentages of dead and deformed chicks, body-weight and organ-weight deficiencies between RFR-exposed and sham-exposed chicks, and adult-bird fertility. Some studies yielded no significant differences between exposed and control groups; in others, significant differences in various endpoints were found, but were ascribable to temperature rises within the eggs during RF exposure

As an example of positive findings, McRee et al. (1983) reported lower fertility and lower sperm motility and counts in quail hatched from fertile eggs exposed to 2.45-GHz CW RFR continuously at 5 mW/cm^2 (mean SAR 4 W/kg) during the first 12 days of incubation. However, the spatial variation of temperature within eggs exposed at relatively high SARs, e.g. 4 W/kg, can be large, thereby yielding spatial-maximum temperatures higher than the basically uniform temperatures within conventionally incubated eggs. Also, Gildersleeve et al. (1987a), in an extension of the McRee et al. (1983) study, investigated the reproductive performance of quail from eggs that had been exposed at the same RFR level during the first 12 days of embryogenesis. The results showed that such exposure during embryogenesis did not affect any of the endpoints they studied, which included: hatchability, mortality after hatching, egg production, egg weight, fertility of the initial groups, and reproductive performance of the progeny. Negative findings were also obtained by Spiers and Baummer (1991).

Studies were done on chicken and turkey eggs by Hills et al. (1974), Fisher et al. (1979), and Saito et al. (1991). Hills et al. (1974) exposed groups of 30 fertile chicken eggs at various stages of development to 6.0-GHz CW RFR at a spatial mean power density of 0.2 mW/cm^2. In another experiment, there were 25 turkey eggs per group. The results showed no significant effect on the hatchability or the growth of chickens or turkeys up to two weeks of age. The exposure methodology and dosimetry aspects of both the Fisher et al. (1979) and Saito et al. (1991) studies were flawed, rendering their findings meaningless.

In summary, exposure to RFR of the eggs or after hatching of various species of birds yielded significant teratogenic effects of various kinds, but only at levels that caused temperature elevations well above those

normally used for incubation. However, no experimental evidence was found to support the hypothesis that RFR is intrinsically teratogenic and there is no evidence that non-thermal RF exposures can be teratogenic

4.4.3 Mice and Hamsters

Many teratogenesis studies were done with mice or hamsters as the subjects, with mixed results. The following are representative examples.

Rugh et al. (1974, 1975) exposed groups of CF-1 female mice to 2.45-GHz RFR at 138 mW/cm^2 (SAR about 123 W/kg) for various durations, and determined that the mean dose (power density x duration) per unit body mass for lethality was about 11 cal/g or 46.1 J/g. Among their findings were fetuses with brain hernia (exencephaly, an effect consistently produced in CF-1 mice by exposure to ionizing radiation). The percentages per litter of fetuses with brain hernia were plotted versus total dose. Exencephaly was absent in at least 45 litters, spanning the total dose range from 3.4 to 7.8 cal/g; 2 litters had 60%, the highest incidence, at about 7 cal/g; and the remainder (about 50 litters) had intermediate percentages, in the range 4.3-7.8 cal/g.

From exposure at a sublethal level [123 mW/cm^2; SAR about 110 W/kg] on the gestation day of highest sensitivity to ionizing radiation, the authors remarked that they could not find any teratogenesis threshold. Reanalysis of their data, however, showed the existence of a threshold: At mean doses less than about 3 cal/g or power densities less than about 1 mW/cm^2, 100% of the fetuses examined were normal. Significant numbers of abnormal fetuses were obtained at RFR levels above that threshold, but the dependence on dose was obscure.

Chernovetz et al. (1975) found that absorption of about 5 cal/g is not teratogenic to mice, a threshold considerably higher than the 3-cal/g value above. In addition, they found that the mean total-dose lethality of the dams was about 5.7 cal/g, an indication that teratogenesis would occur in pregnant mice only at levels that are close to lethality for the dams. Nawrot et al. (1981) found that handling of mice prior to exposure affected the results relative to those for unhandled mice. Their data also indicated that the power-density or whole-body-SAR threshold for teratogenic effects in CD-1 mice is about 30 mW/cm^2 or 40 W/kg.

A study by Stavinoha et al. (1975) involving exposure of mice for 20 minutes to 10.5-MHz, 19.27-MHz, or 26.6-MHz RFR pulses at an electric field strength of 5.8 kV/m showed essentially no differences between mice exposed at each frequency and control mice in subsequent daily weights at corresponding ages up to 21 days.

Berman and coworkers carried out a number of studies, with exposures at power densities up to 28 mW/cm^2 (22.2 W/kg). In Berman et al. (1978), the numbers of litters with one or more anomalous fetuses terms of 10 types of anomalies were tabulated. For most of the specific anomalies, either the numbers of litters affected were too small for statistical treatment or no RFR-related pattern was apparent. Berman et al. (1978, 1982a, 1982b, 1984) found consistently smaller mean body weights of live fetuses from mice and Syrian hamsters exposed to 2.45-GHz RFR at 28.0 mW/cm^2.

In summary, various teratogenic effects have been produced in mice and hamsters by exposure to RFR, but as with birds, only at levels that yielded temperatures elevated well above normal.

4.4.4 Rats

Chernovetz et al. (1977) exposed pregnant rats to 2.45-GHz RFR at 31 W/kg and to infrared radiation (IR) at 47°C to produce the same colonic temperature rise of 3.5°C as the RF exposure. Control rats were sham exposed. The percentages of living fetuses per dam were lower in the RFR group than in the IR and control groups. No structural abnormalities were evident in any of the formed fetuses, but severe edema and hemorrhagic signs were endemic in the IR and RFR groups.

Shore et al. (1977) and Berman et al. (1981) found little evidence for RFR-teratogenic effects in rats, but did find significant deficits in mean body weights of neonates from exposed rats relative to controls. Berman et al. (1981) concluded that the rat is an inappropriate model for determining whether RFR would be teratogenic to humans in exposure situations not lethal for the mothers, and suggested that the mouse is more suitable for that purpose.

Lary et al. (1983) observed teratogenic effects in rats exposed to 27.12-MHz fields (not in the Sutro Tower Digital TV transmitters frequency band) at 55 A/m and 300 V/m (SAR about 11 W/kg), but of severity that increased with colonic temperature. The largest changes were seen for prolonged exposure to maintain colonic temperature at 42.0 °C. The authors ascribed those effects to the hyperthermia induced by the RFR. A subsequent study by Lary et al. (1986) with the same RFR indicated the existence of a colonic temperature threshold of 41.5 °C for birth defects and prenatal death.

Tofani et al. (1986) reported teratogenic effects in rats exposed to 27.12-MHz RFR (not in the Sutro Tower Digital TV transmitters frequency band) at field strengths of 20 V/m and 0.05 A/m (equivalent power density 0.1 mW/cm^2; author-estimated SAR about 0.00011 W/kg). They had characterized the effects as nonthermal and due to long-term exposure, but Lu and Michaelson (1987) took issue with the exposure apparatus and methodology used and with the findings.

Brown-Woodman and Hadley (1988), using two different diathermy units, reported that treatment of pregnant rats to 27.12-MHz RFR (not in the Sutro Tower Digital TV transmitters frequency band) at levels supposedly too low to raise core temperatures with one unit increased the mean number of live embryos and decreased the percentage of resorptions with increasing power, whereas the opposite trends were obtained for treatment with the other unit. Little if any credibility can be given to the finding of non-thermal-RFR-induced teratogenicity in this study, or to a similar study by Brown-Woodman et al. (1988). From the results of a third study, Brown-Woodman et al. (1989) stated: "It would appear that breeding behavior, hormonal cycling and/or the survivability of the eggs before implantation must be affected by the pre-breeding exposure of the rats to RF radiation." However, they did not provide enough data to permit evaluation of their statistical treatment of the results. Also, the lack of adequate dosimetric data (SARs and their temporal and spatial variations), rendered it difficult to ascribe any credibility to their findings.

In the first of a pair of studies, Jounce et al. (1982a) exposed pregnant rats to 915-MHz CW RFR at 10 mW/cm^2 for 6 hours per day on gestation days 1 to 21. The mean SAR over the gestation period was 3.57 W/kg. No statistically significant differences were found between the RFR-exposed and three distinct control groups in mean litter size or mean 21-day-old fetal weight, or in organ-to-body-weight ratios for any of the organs. In Jensh et al. (1982b) [the companion study], half of the initial (F1a) offspring of the exposed and unexposed dams were killed at age 90 days and examined for histopathology. The other rats were cross-bred in various combinations of exposed and control males and females, and the resulting litters

(F2) were examined prenatally for teratogenesis. In the cross-bred females, there were no significant RFR-related differences in mean maternal weight, percentage of resorptions, or in F2 fetal weight or litter size

In the second pair of studies, Jensh et al. (1983a, 1983b) used 2.45-GHz RFR, and obtained similar negative findings. This was also true for Jensh et al. (1984a, 1984b) [the third pair of studies], performed with 6-GHz RFR at 35 mW/cm^2 (about 7.3 W/kg), except for the mean fetal weight at term, which was significantly lower for the RFR group than for the concurrent-control (sham) group. However, the weight differences among the three control groups were also significant, which could indicate that the lower mean fetal weight of the RFR group may not have been RFR-induced. Perhaps the most important finding of these studies was the absence of any terata in F1a, F1b, and F2 offspring from prolonged exposure of rats (8 hours per day throughout their first pregnancy) to 6-GHz RFR

In summary, the only relatively consistent findings in pregnant rats at RFR levels that produced significant body-temperature elevations were the differences in neonate body weight between RFR-exposed and sham-exposed dams, but such findings were not found in all such studies.

4.4.5 Nonhuman Primates

Kaplan et al. (1982), exposed 33 pregnant squirrel monkeys near the beginning of the second trimester to 2.45-GHz RFR within special microwave cavities for 3 hours/day, 5 days/week, until parturition, in which possible effects were sought on mother-offspring behavioral patterns and the EEG. The whole-body SARs were 0.034, 0.34, or 3.4 W/kg (plane-wave equivalent to 0.1, 1, and 10 mW/cm^2). After parturition, 18 of the RFR-exposed dams and their offspring were exposed to the RFR for 6 more months; then the offspring were exposed without the dams for still another 6 months. An unexpected excess of infant deaths occurred, but the total number of animals involved was small. In a subsequent investigation with infant mortality as the basic endpoint, in which enough animals for an adequate statistical treatment of the results were used, the previous finding of an excess of unexpected infant deaths could not be confirmed. The authors did not provide any data, but as stated in a note added in proof to Kaplan et al. (1982), the differences between RFR-exposed and control groups in the numbers of abortions, stillbirths, live births, or infants that subsequently died were not significant.

Taking the RFR-teratogenesis studies collectively, the findings indicate that such effects can occur in both nonmammalian and mammalian subjects from RF exposure, but only at levels that produce significant temperature rises. The results for mammals show that increases in maternal body temperature that exceed specific thresholds (41.5°C in rats) are necessary to cause teratogenic effects. The experimental evidence indicates that RFR is not intrinsically teratogenic and that non-thermal RF exposures are not teratogenic.

4.5 NERVOUS SYSTEM

Concern has been expressed that direct (nonthermal) interactions of RFR with the central nervous system (CNS) could produce deleterious physiological effects. It has been postulated that such effects may be manifested as alterations in behavior, passage of foreign agents from the blood vessels in the brain into the surrounding tissue by opening of the blood-brain barrier (BBB), changes in the histopathology and histochemistry of the nervous system and of the electroencephalogram (EEG), and changes in the efflux of calcium from brain tissue.

4.5.1 Blood-Brain-Barrier Effects

In most organs and tissues of the body, various molecules in the blood can freely diffuse into the tissues around capillaries. However, to protect the brain from invasion by blood-borne microorganisms and toxic substances, the BBB in most regions of the brain allows little or no movement of large fat-insoluble molecules from the blood into the surrounding brain tissues. The BBB can be "opened" by certain agents (such as ionizing radiation or excessive heat) or by chemical substances (e.g., dimethyl sulfoxide). Studies have been conducted to determine if RFR can alter the permeability of the BBB in animals to substances of large molecular weight. The preponderance of negative scientific experimental findings indicates that exposure to pulsed or CW RFR at low levels would not alter the human BBB.

Early studies by Frey et al. (1975) and Oscar and Hawkins (1977) with rats can be disregarded because of evidence of artifacts in the methods used in their experiments. Moreover, Merritt et al. (1978) and Ward and Ali (1985) were unable to reproduce those findings, and Preston et al. (1979) showed that certain specific RFR-induced changes in the brain could be interpreted wrongly as BBB alterations. Preston and Préfontaine (1980) and Gruenau et al. (1982) obtained negative findings regarding RFR-induced alterations of the rat BBB. In several studies, Albert and coworkers used light microscopy and electron microscopy to examine brain slices from hamsters exposed to RFR. The results were questionable because leakage of the tracer used was found in slices from control animals as well as from exposed animals.

Four comprehensive studies by Williams et al. (1984a, 1984b, 1984c, 1984d) in which several different tracers and methods were used for detecting BBB penetration in the rat also yielded negative findings. Neilly and Lin (1986) showed that disruption of the rat BBB at high RFR levels is due to elevation of brain temperature. In addition, they found that high doses of ethanol inhibit BBB disruption by moderating the increases in brain temperature produced by the RFR.

In view of this convincingly negative pattern of results it is therefore surprising to find that a recent study by Salford et al. (1994) reported highly statistically significant effects of 2 hour exposures to rats at SARs between 0.016 and 5 W/kg. Both CW and pulsed waveforms at 915 MHz were used with similar results. Microscopic evidence for leakage across the BBB was scored by an observer who appeared not to be blinded to the treatment condition. Statistically significant results (odds ratio = 3.8, P=0.0004) were reported for all pulse rates (8 to 200 per second) and for CW fields. BBB breakdown showed no dose-response for SARs from 0.016 to 2.5 W/kg, but was more pronounced at 4-5 W/kg. The relatively extreme degree of BBB breakdown found by Salford et al. (1994) and the absence of dose-response suggests greater stress on the exposed animals than was the case in comparable research. Conditions for the control animals were not described and they do not appear to have been treated by sham exposure in the same apparatus as was used for exposure. It is difficult to accept the accuracy of the reported results in view of omissions and deficiencies in the experimental procedure (lack of blinding of the observer, lack of shams, possible thermal or confinement stress to the exposed animals), the high degree of BBB leakage which was inconsistent with similar research, the apparent absence of a defined experimental protocol for the histological and statistical analyses, and uncertain information about actual exposures to brain tissue for the particular test apparatus used.

In summary, the uncertainties in most earlier research on this topic hinge on whether significant artifacts were introduced by the kinds of biological techniques used. For example, the results of several studies have shown that exposure to RFR may alter the size of vascular and extravascular volumes and cerebral blood flow rate, thereby yielding apparent but not real changes in BBB permeability. Much credence can be

given to the findings of more recent studies in which positive controls (known BBB-altering agents) were used. In conclusion, hyperthermic levels of RFR clearly can alter the permeability of the BBB, but there is little or no scientifically reliable evidence that RF exposure at levels that do not increase brain temperature does so.

4.5.2 Neural Tissues: *In Vitro* Studies

RFR effects have been sought in neural tissues excised and kept alive in appropriate solutions while undergoing RF exposure. Courtney et al. (1975) excised superior cervical ganglia from rabbits, immersed each ganglion in a physiological solution, and treated each for alternating 1-minute intervals of exposure and no exposure to 2.45-GHz CW RFR at a power density up to about 300 mW/cm^2 (660 W/kg). During treatment, each ganglion was stimulated with 100-300 μs pulses at 1 pps, and the response latencies for synaptic transmission were measured. No significant differences were found in the mean response latencies measured during and between exposures. Chou and Guy (1978) also obtained negative results with the rabbit vagus nerve and the cat saphenous nerve, as well as the rabbit superior cervical ganglion.

Among histochemical effects sought were RFR-induced alterations in the activities of enzymes acetylcholinesterase (AChE) and creatine phosphokinase (CPK) in rabbit blood. Olcerst and Rabinowitz (1978) found that 2.45-GHz RFR significantly decreased AChE activity, but only at an RFR level sufficient to denature AChE (about 125 mW/cm2). Also, Galvin et al. (1981c) observed that 2.45-GHz RFR did not affect the activity of either AChE or CPK at SARs up to 100 W/kg.

Zakharova et al. (1993) sought effects of amplitude-modulated 900-MHz RFR on spontaneous impulse activity in 500-μm-thick frontal slices of the guinea-pig sensorimotor cortex, and Miura et al. (1993) sought to determine whether exposure of rat-cerebellum preparations to bursts of 10-MHz RFR, each lasting 200 μs and spaced at 200-μs intervals, would increase the production of cyclic GMP. Because of questions on methodology in both studies, little if any credence can be given to their positive or negative findings.

Thus, the findings of the credible studies above were negative except for exposures to clearly thermal RFR levels.

4.5.3 Histopathology and Histochemistry of the Central Nervous System: *In Vivo* Studies

Investigations were also carried out on neural tissues excised from animals after they had been exposed to RFR.

Sanders et al. (1980) found decreases in the concentrations of adenosine triphosphate (ATP) and creatine phosphate (CP) in the rat brain from exposure of rats to 591-MHz CW RFR at 5 or 13 mW/cm^2 relative to those of sham-exposed rats. The difference in results for the two RFR levels was nonsignificant, but they concluded that the changes could not be ascribed to general tissue hyperthermia (but they did not exclude local hyperthermia). Instead, they remarked that the data support the hypothesis that RFR inhibits the electron transport chain function in brain mitochondria, thereby decreasing brain energy levels. Sanders et al. (1984) performed similar experiments, but at 200 MHz and 2,450 MHz as well as at 591 MHz, all at 13.8 mW/cm^2. Local SARs, determined with a non-perturbing probe in the brain of a dead rat during exposure of the carcass, were about 0.6, 2.6, and 5.1 W/kg, respectively. The results for 200 MHz and